IN THE DRAWINGS:

Please amend the drawings as follows:

Replacement sheets of drawings are submitted herewith for the original or previously filed replacement sheets of drawings including Figures 1-3 and 5-17.

REMARKS

I. Status Summary

Claims 1-36 and 38-46 are pending in the present application. Claims 1-36 and 38-46 currently stand rejected by the U.S. Patent and Trademark Office (hereinafter "the Patent Office"). The previously provided corrected drawings have been made the subject of an objection.

Claims 1, 44, 45, and 46 have been amended. Replacement drawings have been submitted. Support for the amendments and replacement drawings can be found in the application as filed. No new matter has been added. Therefore, upon entry of Amendment E, claims 1-36 and 38-46 will be pending in the subject application.

Reconsideration of the application as amended and further in view of the remarks set forth hereinbelow is respectfully requested.

II. Drawing Objections

The Patent Office has required new corrected drawings. More particularly, the Patent Office alleges that the corrected drawings received on May 12, 2009 are not acceptable because Figures 1-3 and 5-16 are not properly labeled with the abbreviation "FIG." The Patent Office further contends that Figure 17 is not properly labeled because each panel needs to be individually labeled.

Replacement drawings for the drawing sheets including Figures 1-3 and 5-16 are being submitted herewith. In the replacement drawings, the label "FIGURE" has been replaced by "FIG." In addition, the left-hand view of Figure 17 has been labeled Fig. 17A, and the "A" previously used to label the left-hand view has been removed. The right-hand view of Figure 17 has been labeled Fig. 17B, and the "B" previously used to label the right-hand view has been removed. Applicants respectfully submit that the replacement drawings comply with 37 CFR 1.121(d). No new matter has been added.

Accordingly, applicants respectfully submit that the Patent Office's objections with regard to the drawings have been addressed. Applicants further submit that the application is in order for allowance and respectfully request a Notice of Allowance to that effect.

III. Response to the Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-36 and 38-46 have been rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to meet the enablement requirement. In particular, the Patent Office contends that, of the five examples provided, Example 5 relates to the claimed invention but no specific starting materials or reaction conditions are described. Further, the Patent Office contends that the claimed method encompasses the detection of multiple target nucleic acids simultaneously but that one would be unable to differentiate which target or targets are present. In this regard the Patent Office notes that claim 45 recites specific reaction conditions, but does not preclude the use of multiple probes against multiple targets and detecting a common nanoparticle. The Patent Office further contends that it, in the methods of claims 1 and 44, one of skill in the art would be unable to differentiate between desired duplex or triplex structures and undesired duplex or triplex structures. The Patent Office contends that one would be un-enabled to use the genus of nanoparticles because a lower limit for the nanoparticle size is not recited. Finally, the Patent Office contends that the specification must enable the use of the product of the method, but that, the claimed method can result in the detection of any nucleotide sequence, including those of unknown sequence and those having no known utility. The Patent Office alleges that in view of the breadth of scope claimed, the limited guidance provided, the unpredictable nature of the art to which the claimed invention is directed, and in the absence of convincing evidence to the contrary, the claims are non-enabled by the disclosure.

After careful consideration of the rejections and the Patent Office's comments, applicants respectfully traverse the rejections and offer the following remarks.

Initially, without acquiescing to the contentions of the Patent Office and in an effort to expedite allowance of the subject application, applicants respectfully submit that claims 1 and 44 have each been amended herein to recite that the nanoparticle has a diameter of between 5 nanometers and 1000 nanometers. Support for the amendment can be found in claims 1 and 44 as previously presented and in the instant specification at page 29, lines 4-11, which recites an upper limit for nanoparticle diameter of about 1000 nanometers and that in some embodiments, the lower limit for the diameter is about 5 nanometers.

In addition, claims 1, 44, and 45 have been amended to recite that the capture probe hybridizes specifically to the target nucleic acid. Support for the amendments can be found in the claims as previously presented and in the instant specification at page 37, lines 17-20, which recites that "specifically hybridizes" refers to hybridizing only to a particular nucleotide sequence when that sequence is present in a complex or heterogeneous mixture. Additional support can be found in the instant specification at page 38, lines 15-16.

In view of the amendments to claim 1, claim 46 has been amended herein to recite wherein the sample comprises a heterogeneous nucleic acid mixture.

Applicants respectfully submit that the "test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." See Manual of Patent Examining Procedure (hereinafter "MPEP") § 2164.01, citing *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). The scope of enablement must only bear a reasonable correlation to the scope of the claims. See MPEP § 2164.08, citing *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Claims are not to be rejected as broader than the enabling disclosure under 35 U.S.C. § 112, for noninclusion of limitations dealing with factors which must be presumed to be within the level of ordinary skill in the art; the claims need not recite factors one of ordinary skill in the art would consider obvious. See MPEP § 2164.08 citing *In re Skrivan*, 427 F.2d 801, 806, 166 USPQ 85, 88 (CCPA 1970). Further, "it is not necessary to enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim limitation to that effect." See MPEP § 2164, citing *CFMT, Inc., v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1338, 68 USPQ2d 1940, 1944 (Fed. Cir. 2003). Additionally, applicants respectfully submit that if a statement of utility in the specification contains within it a connotation of how to use, 35 U.S.C. § 112 is satisfied. See MPEP § 2164.01(c), citing *In re Johnson*, 282 F.2d 370, 373, 127 USPQ 216, 219 (CCPA 1960); and *In re Hitchings*, 342 F.2d 80, 87, 144 USPQ 637, 643 (CCPA 1965).

With particular regard to the Patent Office's contentions regarding the examples, applicants respectfully note that the specification need not contain an example if the

invention is otherwise disclosed in such manner that one skilled in the art is able to practice it without undue experimentation. See MPEP § 2164.02, citing *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). Notwithstanding this, applicants respectfully note that while Example 5 deals specifically with the detection of a change in temperature related to the presence of DNA/gold nanoparticle complexes, Example 1 provides teachings with regard to specific starting materials for providing the DNA/gold nanoparticle complexes. For example, Example 1 describes specific attachment chemistry for a single stranded DNA (e.g., a capture probe) to an indium tin oxide (ITO) substrate. Example 1 further describes that complementary 18 base pair sequences (e.g., a complementary capture probe and target nucleic acid pair) were attached to ITO and 10 nm diameter gold nanoparticles. See Instant Specification, page 57, lines 30 to page 58, lines 20. Hybridization conditions are specifically provided for sequences of a range that includes 18 base pairs in the instant specification at page 39, lines 1-4.

With respect to the Patent Office's contentions regarding the detection of multiple target nucleic acids in a simultaneous manner using a single nanoparticle (e.g., a single type of nanoparticle), applicants respectfully note that the instant specification provides significant teaching as to ways in which multiple target nucleic acids can be detected according to the presently disclosed methods. For example, applicants respectfully note that the instant specification, at pages 24-25, describes that in some embodiments, a plurality of capture probes (i.e., a plurality of different capture probes) can be attached to a solid surface in an array format, wherein each capture probe has a unique, identifiable location on the surface. This concept is engendered in dependent claim 21. Hybridization can then be detected at each capture probe attachment point by detecting thermal variation across the entire surface. See Instant Specification, page 57, lines 15-17.

In some embodiments, determining whether hybridization has occurred at any particular capture probe attachment site can be accomplished by irradiating individual array elements separately, as recited in claim 22. In some embodiments, an entire array can be irradiated and an IR detector can scan the array, by either repositioning of the detector or the substrate surface. See Instant Specification, page 46, lines 17-19. Thus, the presence or absence of a hybridization complex at each capture probe

attachment site can be determined by sequential temperature detections at multiple individual array positions.

The instant specification further describes how the IR spectra of multiple array elements can be determined in parallel, for example, by using a high-speed IR camera with a focal plane array. See Instant Specification, page 51, lines 20-30. In such cases, a single IR image can show temperatures at different array positions at the same time. For example, the image shown in Figure 15 of the subject application shows an image where the temperatures at various positions on a single substrate are provided. The areas of greatest temperature increase are the areas where more nanoparticles (i.e., a higher concentration of nanoparticles) are attached. Figure 14 of the subject application also associates specific positions on a single substrate with specific temperature increases, thereby allowing for the correlation of nanoparticle concentration with substrate position.

Applicants respectfully submit that based on the wording of claim 1, the concentration of hybridization complex can be directly proportional to nanoparticle concentration and, thus, to target nucleic acid concentration. See also Instant Specification, page 12, lines 25-27. Accordingly, applicants respectfully submit that one of ordinary skill in the art could recognize that one could detect temperature differences at different array attachment positions in a site specific manner to determine the presence and/or concentration of hybridization complexes at a specific site or sites and correlate the array position to particular capture probe sequences, and therefore, to the corresponding complementary target nucleic acid sequences, particularly in view of Figure 16 and Example 5 on page 62 of the instant specification. While claim 1 does not specifically recite whether exposing the solid surface to light is done via rastering or whether the temperature detection is done in a site-specific manner, applicants respectfully submit that, in view of the teachings of the instant specification, such as described directly hereinabove, and in view of the fact that claim 1 also encompasses embodiments wherein only a single capture probe is used to detect a single target nucleic acid, such recitation is not necessary to fulfill the enablement requirements of U.S.C. § 112, first paragraph.

With regard to the Patent Office's comments regarding the phrase "selectively hybridizes," applicants respectfully submit that as noted in the instant specification and in the amendment filed in the instant application on May 12, 2009, selective hybridization refers to the hybridization of a molecule (e.g., a capture probe) to a particular nucleotide sequence (e.g., a specific target nucleic acid or a segment thereof). See Instant Specification, page 37, lines 17-20 and page 39, lines 5-11. For example, selective hybridization can involve the use of stringent conditions when the target is present in a complex or heterogeneous mixture. See Instant Specification, page 21, lines 15-18 and page 37, line 29 to page 39, line 16. The instant specification describes that stringent hybridization conditions are those that can preclude hybridization of random, non-complementary sequences (e.g., non-target sequences). Applicants further respectfully submit that no undue experimentation would be required by one of ordinary skill in the art to vary the hybridization conditions to provide selective hybridization in view of the level of ordinary skill in the art as well as guidance in the instant specification that the hybridization conditions can be varied, particularly based on the lengths of the nucleic acid sequences involved (i.e., the lengths of probe and target), the base content of the sequences, and the presence of other compounds. See *Id.* However, while applicants believe that "selectively hybridizes" was more than sufficient to enable the use of the presently disclosed claims, applicants note that claims 1 and 44 has been amended as described directly hereinabove in an effort to expedite their allowance to specifically recite that providing the hybridization complex is performed under conditions wherein the capture probe hybridizes specifically to the target nucleic acid.

With regard to the Patent Office's comments with respect to the recitation that the capture probe is "complementary in whole or in part to the target nucleic acid," applicants respectfully submit that, as noted in the Amendment filed in the subject application on May 12, 2009, the specification describes embodiments wherein the probe comprises an oligonucleotide that is complementary to a contiguous nucleic acid sequence of a target nucleic acid (i.e., to a nucleotide sequence that is one segment of the entire target nucleic acid) such that the oligonucleotide (i.e., the capture probe) specifically hybridizes to the target. See Instant Specification, page 21, lines 15-19 and

page 36, lines 6-9. Further, the instant specification provides guidance with regard to the use of sandwich format hybridization assays wherein the capture probe comprises an oligonucleotide complementary to a first domain (i.e., one segment) of the target nucleic acid and a nucleotide-containing detection probe is complementary to a second, non-overlapping domain (i.e., a second segment) of the target. See Instant Specification, page 15, line 24 to page 16, line 2; page 36, lines 19-33; and Figure 1. Accordingly, applicants respectfully submit that the instant specification as filed provides enablement with regard to embodiments wherein the capture probe is not complementary in whole to the target nucleic acid.

Concerning the Patent Office's comments regarding nucleic acid length, applicants respectfully submit that the overall length of the target nucleic acid can be any length, as long as the hybridization complex can be provided. Determining whether a particular target nucleic acid can be detected according to the presently claimed method would merely require routine experimentation. Applicants respectfully submit that the recitation in each of independent claims 1, 44, and 45 that a hybridization complex is provided and that the capture probe hybridizes specifically to the target nucleic acid precludes any non-working embodiments. With regard to the term "nanoparticle," applicants respectfully submit that, as noted hereinabove, claims 1 and 44 have been amended to include a lower limit for the nanoparticle diameter in an effort to expedite allowance. Further, applicants respectfully submit that the term "nanoparticle" is well known in the art and the instant specification provides significant guidance as to nanoparticles at, for example, page 28, line 27 to page 32, line 22.

Finally, applicants respectfully disagree with the Patent Office's contention that the instant specification is silent with regard to how the information of detection is to be used. As noted in the Amendment filed in the subject application on July 28, 2008, in response to the rejections under 35 U.S.C. § 101, applicants respectfully submit that the instant specification recites that the detection of nucleic acids, such as by the presently claimed methods, can be part of numerous techniques, including, for example, gene identification, mutation detection, gene expression profiling, and DNA sequencing. The instant specification also notes that diagnostic and forensic applications are but two

areas in which nucleic acid detection techniques find use. See Instant Specification, page 1, lines 22-26.

Moreover, the instant specification notes that the methods concern a photothermography system for detecting specific target sequences by using oligonucleotide probes that are specific for identifying segments of such. As described in the instant specification, if there is an identifiable sequence (i.e., if there is a specific, known nucleic acid sequence that forms at least a part of the target nucleic acid), diagnostic assays such as for aberrant chromosomal variations, cancers and genetic abnormalities can be facilitated by the presently disclosed methods. See Instant Specification, page 54, lines 13-22. Accordingly, applicants respectfully submit that one of skill in the art would understand that if a particular disease (e.g., a cancer or a disease associated with a genetic mutation or other abnormality) is known to be associated with the presence of a specific target nucleic acid, detecting that target nucleic acid via the presently disclosed methods can serve to diagnose the disease. Knowledge of the presence of a particular known target nucleic acid in a sample can also be used to diagnose or monitor a viral or bacterial disease (e.g., in checking for the presence of a particular target sequence associated with a particular virus or bacteria), in forensics, paternity testing, or cell line authentication (e.g., in checking for the presence of a target nucleic acid associated with a particular crime suspect, potential parent, or known cell line) or in monitoring gene therapy (e.g., in checking for the presence of a target nucleic acid associated with an exogenous, therapeutic nucleic acid in the cells of a gene therapy patient). For further information in the instant specification with regard to how detecting a particular target sequence can provide information regarding an infection (e.g., of a virus or bacteria) please see Instant Specification, page 15, lines 9-16.

In addition, the instant specification describes in detail how the presently disclosed methods can be used in a method of monitor gene expression at page 55, lines 6-26. Further, the instant specification describes in detail how the presently disclosed methods can be used to detect mutations at page 55, line 29 to page 56, line 18. The instant specification describes how the presently disclosed methods can be used in probe design at page 56, line 19 to page 57, line 5.

Accordingly, particularly as the Patent Office has not provided a reasonable scientific justification for why one of ordinary skill in the art would not be able to make use of the information obtainable by the presently claimed methods, applicants respectfully submit that the instant specification, both by generally describing instances wherein knowledge of the presence of a particular nucleic acid and by describing in more detail how the presently disclosed methods can be adapted to certain situations (e.g., monitoring gene expression), meets the requirements of 35 U.S.C. § 112, first paragraph with regard to enabling the use of the presently claimed subject matter.

Accordingly, applicants respectfully request that the rejections of claims 1-36 and 38-46 under 35 U.S.C. § 112, first paragraph, be withdrawn. Applicants respectfully ask that claims 1-36 and 38-46 be allowed at this time.

CONCLUSION

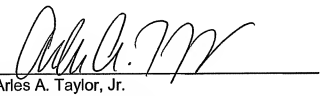
In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any additional fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,
JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: December 22, 2009 By: 

Arles A. Taylor, Jr.
Registration No. 39,395
Customer No. 25297
(919)493-8000

297/178/2 AAT/ALO/cam

Enclosures